Remarks

Claims 1 and 9 have been amended. Claims 2-4, 10 and 11 are canceled. Claims 5-8 were previously withdrawn.

Claim 10 is indicated in the Office Action Summary as withdrawn but is rejected on office action pages 2 and 5. Claim 11 is indicated in the Office Action Summary as rejected but is not rejected in subsequent office action pages. Applicants assume Claim 11 is withdrawn and Claim 10 is rejected. Both are now canceled.

Claim 1 has been amended to incorporate the limitations of dependent Claims 2-4 into Claim 1. Claim 9 has been amended to incorporate the limitations of dependent Claims 10 and 11. Entry of the amendments is respectfully requested.

Claims 1, 9 and 10 were rejected under 35 USC 102(b) as anticipated by Donahue, et al.

Donahue, et al., describe gene therapy methods for treating and preventing cardiac arrhythmia. The method involves administration of polynucleotides. With the amendments of Claims 1 and 9 described above, Applicants respectfully maintain that the claims are not anticipated by Donahue, et al. Reconsideration and withdrawal of the rejection is respectfully requested.

Claims 1-4, 9 and 10 were rejected under 35 USC 103(a) as unpatentable over Pugsley, et al., and Gehrmann, et al., in view of Knobloch. Applicants respectfully maintain that the invention claimed in amended Claims 1 and 9, which provides an electrophysiology profile of a compound, to determine the extent of significant off-target activity of the compound, without the need for an invasive cardiac electrophysiologic method, by measuring one or more of the arterial refractory period, ventricular refractory period and AV nodal refractory period, and one or more intervals including an electrocardiogram interval and a cardiac electrogram conduction interval, is not obvious in view of the cited references.

Pugsley, et al., describe a method for evaluating actions, on the cardiovascular system and on the myocardial ionic currents in rats, of the selective kappa receptor agonist spiradoline. Drug is administered into the cannulated right jugular vein, and blood pressure effects are measured and recorded in the cannulated left carotid artery. Electrical stimulation of the left ventricle was accomplished via insertion through the chest wall of 2 Teflon coated silver wire stimulating electrodes into the left ventricle.

In the claimed invention, drug is administered into the cannulated left femoral artery, and a catheter is inserted into the left femoral artery to measure blood pressure. A third catheter, inserted into the right femoral vein, is used to administer ketamine:xylazine. A fourth recording and stimulating catheter is inserted into the right jugular vein and advanced

to the near right atrium. A fifth recording and stimulating catheter is inserted into the common carotid of the rat. Two electrodes are used to obtain bipolar ventricular and His bundle electrograms, and two are used to pace the ventricle. Needle electrodes are subcutaneously placed at the right axillary and left inguinal areas of the rat.

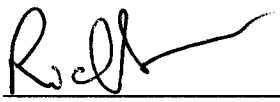
Applicants respectfully maintain that the claimed procedure differs from the one described by Pugsley, et al. to provide significant off-target activity information. Puglsley, et al., administer drug and measure blood pressure in vessels that are distinct from those used by the present invention.. Additionally, Pugsley, et al., do not administer recording and stimulating catheters into the right jugular vein and common carotid of the rat. Pugsley, et al., do not suggest different vessels for administration of drug and measurement of blood pressure. Accordingly, the claimed procedure would not be obvious a person having ordinary skill in the art in view of Pugsley, et al.

Furthermore, Pugsley, et al., in combination with Gehrmann, et al., and Knobloch would not make the claimed invention obvious.

Gehrmann, et al., describe electrophysiologic studies in genetically engineered mice. In the epicardial study, wires are placed on the right ventrical, left ventrical, and right atrium. In the intracardial study, a catheter is advanced from the right internal jugular vein through the right atrium to the right ventrical. Knobloch describes a study of a selective human cardiac ultrarapid delayed rectifier potassium current blockers in pigs. Applicants maintain Gehrmann, et al., and Knobloch, in combination with Pugsley, et al., would not lead a person having ordinary skill in the art to the specific procedure of the claimed invention.

Reconsideration and withdrawal of the rejections under 35 USC 102(b) and 35 USC 103(a) is respectfully requested.

Respectfully submitted,



Richard S. Parr, Reg. No. 32,586
Attorney for Applicant

MERCK
P.O. Box 2000
Rahway, New Jersey 07065-0900
Tel.: (732) 594-4958

Date: October 1, 2010